REMARKS

Applicant respectfully requests entry and consideration of the foregoing amendments and the following commentary before continued examination of the present application.

I. Status of the Claims

Claim 1 has been amended to set forth more clearly what Applicant intends to claim as his invention. Claims 2-12 have been cancelled, without prejudice or disclaimer, and replaced by new claims 13-29. The original specification provides ample support for these changes. See page 3, last full paragraph, and succeeding paragraphs, for example.

Upon entry of this amendment, claims 1 and 13-29 will be pending.

II. Overview of the Invention

At the outset, Applicant would emphasize that total cholesterol subsumes cholesterol in low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), and chylomicron (CM). Accordingly, the present recitation of "cholesterol in lipoproteins other than LDL" encompasses cholesterol in HDL, VLDL and CM. See also specification at page 2, second paragraph, and page 7, last full paragraph.

The claimed invention relates to measuring LDL and the total cholesterol in a single assay. The methodology of the invention entails a first step, measuring cholesterol other than LDL (i.e., cholesterol in HDL, VLDL and CM), and a second step, measuring total cholesterol. Thus , the difference between the two measurements constitutes the amount of LDL in "the biological sample."

The present invention is depicted in Figure 1 of the application. In particular, a compound is generated in the presence of a first reagent that acts only on the cholesterol in lipoproteins other than LDL, and the amount of the compound is determined by the absorbance at a certain wavelength optimal for that compound. This first measurement value reflects the

amount of the cholesterol in lipoproteins other than LDL, including , as noted, HDL, VLDL and CM.

Subsequently, a second reagent that acts on at least LDL is added to react with the remaining LDL in the sample and to generate an additional amount of the compound. By virtue of this additional amount, the absorbance at this wavelength is increased. The total absorbance value therefore represents the amount of total cholesterol, while the difference between these two measurements represents the amount of LDL in the sample.

III. Rejection of Claims under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-12 for alleged obviousness over U.S. patent 6794157 to Sugiuchi. Although the rejection is moot as to cancelled claims 2-12, Applicant submits that claims 13-29 are patentable over Sugiuchi, along with claim 1, for reasons discussed here.

Sugiuchi describes determining the concentrations of ***HDL*** cholesterol and the total cholesterol in an assay. The Sugiuchi method cannot illuminate the amount of LDL in a sample, because subtracting the amount of HDL from the total cholesterol will only result in the amount of cholesterol in LDL, VLDL, and CM.

By contrast, the claimed invention is directed to determining the amount of ***LDL*** and the total cholesterol in one assay by measuring the amount of ***cholesterol in lipoproteins other than LDL, which include HDL, VLDL and CM,*** and the total cholesterol. Therefore, the amount of LDL is reflected by the difference between the first measurement and the second measurement.

With reference to Sugiuchi at column 10, lines 16-28, as well as at column 12, lines 38-49, the Examiner asserts that the reference "teaches a method wherein the first step comprises reacting cholesterol in lipoproteins other than LDL in a biological sample, and a second step in which cholesterol in the remaining LDL is reacted" (page 3, second and third paragraphs). To the contrary, however, the Sugiuchi patent actually teaches that HDL cholesterol and LDL cholesterol "are fractionally determined"; that is, the amount of HDL is first determined, and then

reagent A, which "act[s] ***only*** on LDL cholesterol," is added to determine the amount of LDL (column 4, line 65 to column 5, line 2; emphasis added).

Thus, the Examiner errs in his understanding of Sugiuchi's first step, which determines HDL ***only*** but not "cholesterol in lipoproteins other than LDL." The Examiner also mischaracterizes the second step of Sugiuchi by stating that "cholesterol in the ***remaining*** LDL is reacted." Because LDL, VLDL and CM are all remaining in the sample after the first step, the amount of LDL is ***selectively*** determined, pursuant to Sugiuchi.

Accordingly, the Examiner is heard to equate HDL, incorrectly, with "cholesterol in lipoproteins other than LDL." As explained above, "cholesterol in lipoproteins other than LDL" includes HDL, VLDL and CM.

These factual errors undercut the stated grounds for alleged obviousness. The Examiner also errs in referring to column 21 of Sugiuchi for a teaching of "a surfactant acting on lipoproteins other than LDL" (final action, page 4, lines 1-2). To the contrary, the cited patent never discloses a reagent that "act[s] on lipoproteins other than LDL." As Applicant has noted, a reagent that acts on lipoproteins other than LDL should react with HDL, VLDL and CM. In fact, Sugiuchi describes three reagents: reagent A, which "act[s] ***only on LDL***" (column 4, line 66 to column 5, line 2); reagent B, which "act[s] ***only on HDL***" (column 5, lines 7-8); and reagent C, which "act[s] on ***cholesterol in all lipoproteins***" (column 5, lines 17-19). Furthermore, Sugiuchi discloses that the reagents or the enzymes are employed depending on their specificity to the substrate (column 7, last paragraph).

It is apparent, therefore, that the skilled artisan would have appreciated Sugiuchi's combination of the reagents could not have been used to measure the cholesterol in lipoproteins other than LDL, thereby determining the amounts of LDL and total cholesterol in one assay. In contrast, the present invention describes that the cholesterol esterase produced by bacteria Pseudomonas, in the presence of a surfactant, acts on cholesterol in lipoproteins other than LDL (specification, page 11, line 24).

The Examiner acknowledges that the cited patent "does not teach the simultaneous measurement of LDL and total cholesterol in a biological sample" (final action, page 5, last paragraph). Nevertheless, he advances the proposition, without cited support, that "it would have been obvious...to adapt the methods of Sugiuchi" to arrive at the invention (final action, page 6, first paragraph).

According to MPEP § 2143, a *prima facie* case of obviousness has three prerequisites. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, a reference or combination of references must teach or suggest all the claim limitations.

Applicant submits that the Examiner fails to establish a *prima facie* case of obviousness, because (A) the cited patent does not suggest that LDL and the total cholesterol can be measured in one assay, (B) the reagents taught by Sugiuchi could not have yielded a measurement of LDL and total cholesterol in one assay, and, in any event, (C) the cited patent does not teach or suggest step (i) of the claimed method. Accordingly, the obviousness rejection should be withdrawn.

Claims 22 and 24 recite an albumin, which is not taught or suggested by the cited art. Therefore, claims 22 and 24 are patentable in their own right, as well as for the reasons set out above.

CONCLUSION

In view of the foregoing, all pending claims are deemed patentable over the cited art, and Applicant therefore requests withdrawal of the rejection. Applicant further submits that the application is in condition for allowance.

An early indication to this effect is requested. To this end, the Examiner is invited to contact the undersigned to discuss any issue that he feels warrants further consideration.

The Commissioner is hereby authorized to charge any additional fees, which may be required regarding this application under 37 CFR §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit. If any extensions of time are needed for timely acceptance of submitted papers, Applicant hereby petitions for such extension under 37 CFR §1.136 and authorizes payment of any such extensions fees to the deposit account.

Respectfully submitted,

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By S. A. Bent

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5404
Facsimile: (202) 672-5399

Stephen A. Bent
Attorney for Applicant
Registration No. 29,768